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The design of a Social Cost-Benefit Analysis of preventive interventions for toxoplasmosis: An example of the One Health approach

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Summary

Toxoplasma gondii infections cause a large disease burden in the Netherlands, with an estimated health loss of 1,900 Disability Adjusted Life Years and a cost-of-illness estimated at €44 million annually. Infections in humans occur via exposure to oocysts in the environment and after eating undercooked meat containing tissue cysts, leading to asymptomatic or mild symptoms, but potentially leading to the development of ocular toxoplasmosis. Infection in pregnant women can lead to stillbirth and disorders in newborns. At present, prevention is only targeted at pregnant women. Cat vaccination, freezing of meat destined for undercooked consumption and enhancing biosecurity in pig husbandries are possible interventions to prevent toxoplasmosis. As these interventions bear costs for sectors in society that differ from those profiting from the benefits, we perform a social cost-benefit analysis (SCBA). In an SCBA, costs and benefits of societal domains affected by the interventions are identified, making explicit which stakeholder pays and who benefits. Using an epidemiological model, we consider transmission of *T. gondii* after vaccination of all owned cats or cats at livestock farms. To identify relevant high-risk meat products that will be eaten undercooked, a quantitative microbial risk assessment model developed to attribute predicted *T. gondii* infections to specific meat products will be used. In addition, we evaluate serological monitoring of pigs at slaughter followed by an audit and tailor made advice for farmers in case positive results were found. The benefits will be modelled stochastically as reduction in DALYs and monetized in Euro's following reference prices for DALYs. If the balance of total costs and benefits is positive, this will lend support to implementation of these preventive interventions at the societal level. Ultimately, the SCBA will provide guidance to policy makers on the most optimal intervention measures to reduce the disease burden of *T. gondii* in the Netherlands.

KEYWORDS

cat vaccination, freezing meat, prevention, risk assessment, social cost-benefit analysis, toxoplasmosis

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1 | INTRODUCTION

Toxoplasmosis is caused by the protozoan parasite *Toxoplasma gondii*. This parasite can infect a wide range of warm-blooded animals such as birds, mice, rats, cats, sheep, pigs and cattle, as well as humans. Most species function as intermediate hosts, and they will not shed *T. gondii* in the environment, but infection will lead to the development of infectious tissue cysts. Cats and other felids function as definitive hosts, meaning that *T. gondii* can complete its sexual cycle resulting in shedding of millions of oocysts in their faeces for up to three weeks (Dabritz & Conrad, 2010). These oocysts can remain viable in the environment for about a year (Dumetre & Darde, 2003; Frenkel, Ruiz, & Chinchilla, 1975), where they can infect other animals, both farm and non-farm animals as well as humans. Infections in humans occur mostly via exposure to oocysts in the environment or after eating raw or undercooked meat containing tissue cysts, often leading to an asymptomatic infection or mild flu-like symptoms (Elmore et al., 2010), but potentially leading to the development of ocular toxoplasmosis (Weiss & Dubey, 2009). Besides, toxoplasmosis is also well-known as a cause of congenital disease in humans. Infection in naïve pregnant women can lead to abortion, stillbirth and serious disorders in newborns such as hydrocephalus, microcephalus and chorioretinitis later in life (Weiss & Dubey, 2009).

As a consequence of these serious health risks, *T. gondii* is an important pathogen in terms of burden of disease in humans in the Netherlands. The burden of toxoplasmosis can be distinguished into the number of years of life lost (premature mortality) and the number of years lived in less than full health (morbidity). The aggregate of both measures is a quantification of the years of healthy life lost due to a certain disease or infection, better known as the Disability Adjusted Life Years (DALYs). It is recently estimated that toxoplasmosis is responsible for a disease burden (undiscounted) of about 1,903 DALYs per year (Mangen, Friesema, Haagsma, & Van Pelt, 2017). With this disease burden, *T. gondii* ranks third among all foodborne-related pathogens, after *Campylobacter spp.* that is associated with 3,573 DALYs and norovirus with 2,248 DALYs in the Netherlands (Mangen et al., 2017). In 2016, the estimated mean annual number of infections of toxoplasmosis in the Netherlands was 767, of which 344 were congenital and 423 were acquired in later life (Mangen et al., 2017). In the same year, the estimated mean annual number of deaths was 12. About half of all toxoplasmosis-related DALYs are associated with congenital toxoplasmosis. Mangen et al. (2017) assessed the cost-of-illness of toxoplasmosis in 2016 at € 44 million, considering disease-related costs from a societal perspective, which means that in addition to health care costs, also productivity losses due to work absence of caregivers and patients and the cost of special education were included. In order to reduce the burden of disease and associated costs, additional strategies to prevent both congenital and acquired toxoplasmosis in the population should be considered.

In the Netherlands, toxoplasmosis prevention currently is only targeted at educating and counselling pregnant women (Opsteegh, Kortbeek, Havelaar, & van der Giessen, 2015). No intervention is

Impacts

- *Toxoplasma gondii* infections cause a large disease burden in the Netherlands, with an estimated health loss of 1,900 Disability Adjusted Life Years and a cost-of-illness estimated at €44 million annually.
- Three possible preventive interventions: cat vaccination, freezing meat destined for undercooked consumption and enhancing biosecurity in pig husbandries bear costs for stakeholders in society that differ from those profiting from benefits.
- In a social cost-benefit analysis (SCBA), all costs and benefits are identified, making explicit which stakeholder pays and who benefits. The results of the SCBA will guide policy making. If the balance of costs and benefits is positive, it will lend support to implementation of these preventive interventions.

applied in the food chain. Opsteegh et al. (2015) Opsteegh described that cat vaccination, freezing of meat destined for raw or undercooked consumption and enhancing biosecurity in pig husbandries are potential interventions to further prevent *T. gondii* infections. Implementation of these interventions would most likely reduce the number of infections, but increase costs in several domains of society at the same time. Toxoplasma infections in animals are generally asymptomatic, preventing infections in animals which result mostly in additional costs. However, there are some additional benefits for the farmers/food chain, such as a reduction in abortions in ewes when implementing the cat vaccination intervention and less spilled feed due to rodent control when increasing biosecurity at pig farms. Freezing high-risk meat products has economic consequences for both the meat processing industry and consumers of the high-risk meat products. There may be a disbalance between stakeholder groups that have to pay for these interventions and stakeholder groups that will benefit from such interventions.

A social cost-benefit analysis (SCBA) is an established method to map the distribution of the short-term and longer-term costs and benefits of implementing new interventions over the different stakeholders involved in these interventions. Performing an SCBA implies the identification and valuation of all costs and all benefits of a certain intervention in monetary terms. The valuation of the costs and benefits in an SCBA allows comparison and ranking of the results of the various interventions (Romijn & Renes, 2013). Within an SCBA, the overall sum of benefits and costs is reported as net social costs or net social benefit. This is the sum of all the valued benefits minus the sum of all the valued costs. If the monetized balance of the total costs and total benefits is positive, then this will lend support to implementation of these preventive interventions at the societal level. By allowing a ranking of these net social benefits of different interventions, the SCBA will help to decide which intervention is most worthwhile to be implemented.

SCBAs are rarely performed when evaluating interventions affecting both human and animal health. Most evaluations focus either on the stable to slaughterhouse (animal health), or on public health domains and ignoring the other sectors. There are a few exceptions; some economic evaluations of zoonosis included a range of social costs and effects. For example, Sundstrom, Wahlstrom, Ivarsson, and Sternberg Lewerin (2014) assessed the net benefits of introducing alternative *Salmonella* control strategies taking expected changes in human and cattle morbidity and the associated monetary effects into account. Quality of life loss due to salmonellosis could not be incorporated into the model. Babo Martins, Rushton, and Stark (2016, 2017) evaluated the economic effects of zoonosis surveillance. In the case of *Campylobacter*, costs of an animal and human monitoring system were included. In another economic evaluation, the social costs and effects of combined rabies control interventions such as dog vaccination, and pre- and post-exposure prophylaxis in humans were assessed (Hasler et al., 2014). Unlike our study, in the latter two studies, the benefits were not monetarized in Euros but only expressed in human infections and DALYs averted. Within health care, most economic evaluations concern cost-effectiveness analyses (CEAs). In a cost-effectiveness study, a scenario with a new intervention is often compared to a scenario without this intervention (mostly the current situation), and sometimes several interventions are compared among each other. In a CEA, the incremental cost-effectiveness ratio (ICER) shows the net costs of health improvement, for example in terms of costs per Life Year Gained (LYG) or DALY averted of the new intervention, compared to care as usual or to not implementing that intervention. Although most guidelines for economic evaluation advocate the use of a societal perspective, in reality many analyses use a health care perspective (Belli, Anderson, Barnum,

Dixon, & Tan, 1998, ZIN, 2015). In case a societal perspective is taken, this often is limited to the inclusion of productivity losses and additional patient costs, such as travel costs. Wider societal costs, such as those for the food production industry, are not taken into account in general. In addition, CEAs pay little attention to distributional aspects, regarding the stakeholders who pay for an intervention and who get the benefits. In contrast to CEAs, health benefits in SCBAs are expressed in a monetary unit (e.g. dollars or Euros), and not in a specific health outcome, such as DALYs or infections averted (Koopmans et al., 2016a,b; Romijn & Renes, 2013; Treasury, 2015). The SCBA requires availability of data from all relevant domains. A well-performed SCBA is attractive because it takes into account both the inter-sectoral costs and benefits as well the distributional issues since the interventions impact several domains of society.

The aim of this article is to present the design of an SCBA investigating the costs and (monetarized) benefits of three preventive interventions with the objective to reduce the disease burden of toxoplasmosis in the Netherlands: (i) cat vaccination, (ii) freezing of high-risk meat products from cattle, pigs and sheep, (iii) enhancing biosecurity on pig farms. Since SCBA is rarely applied in the field of zoonoses research, the design of such an approach might be of interest for all working in the One Health community.

2 | METHODOLOGY OF A SOCIAL COST BENEFIT ANALYSIS

For Dutch government decisions that involve several domains of society, SCBA is the recommended analytical technique. The study will be performed according to the Dutch general guidelines for SCBAs

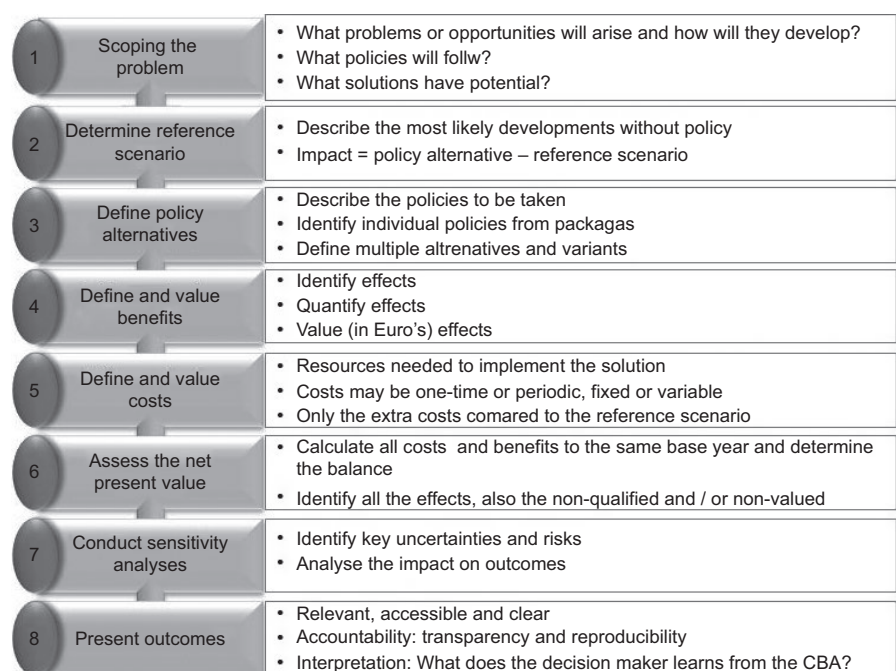


FIGURE 1 Research steps of a Social Cost-Benefit Analysis (adapted from (Romijn & Renes, 2013))

and will follow steps recommended in these guidelines (see Figure 1) (Romijn & Renes, 2013; Koopmans et al., 2016b,a).

As shown in Figure 1, the guideline prescribes 8 steps that will be explained below.

2.1 | Step 1 scoping the problem

In this first step, the initial situation with regard to the problem at hand is determined. What is the size of the problem? What is the prevalence and incidence of toxoplasmosis, both in the animal and the human population, what are the consequences of toxoplasmosis in terms of disease burden in humans, and what are the consequences of toxoplasmosis in animals, if any, and what will be the trend into the future under the current interventions? Will the problem diminish, increase or stabilize and what are the main drivers for these future trends? The main aim of this step is to portray the current state of affairs (including the main actors) for toxoplasmosis in the Dutch society. This step also includes an inventory of current interventions to prevent toxoplasmosis.

2.2 | Step 2 the reference scenario

In this step, the reference scenario will be described in terms of costs and consequences of continuing current interventions (unchanged policies). Essentially, this is limited to creating awareness among pregnant women and advising on preventive measures that pregnant women can take themselves. No other interventions are currently in place, neither in the public health domain, nor at the farm or in the food chain. At the start of the project, all relevant stakeholders are identified based on information from websites, grey and scientific literature and on interviews with experts in the field and from scientific institutes (EFSA, 2011a,b, Kotula et al., 1991; Opsteegh, Kortbeek, & Giessen, 2011; Torgerson & Macpherson, 2011; Verma & Khanna, 2013) (Table 1). Human health care, agriculture in particular livestock holders, veterinarians, animal feed companies, food processing industry and education are involved with the interventions under study. The stakeholders will experience a change in costs and benefits due to the interventions. Furthermore, higher or lower prices will influence the producer and consumer surplus. A crucial assumption is that we assume that interventions will be supported and adopted by all European countries. Therefore, we do not take into account import of non-frozen meat from abroad, nor the jeopardy for competitiveness should only one European country require food industry to freeze certain types of meat. Ultimately, the net benefits per stakeholder are presented. Defining the reference scenario is crucial, because this will be the scenario to which the costs and benefits of new interventions will be compared.

2.3 | Step 3 define the interventions

People can become infected via three main ways of transmission: ingesting uncooked meat containing tissue cysts, ingesting food

and water contaminated with oocysts from infected cat faeces, and congenitally (Opsteegh et al., 2015). Since an effective human vaccine is lacking, prevention of zoonotic transmission from animals or environment to humans is therefore the most optimal alternative. Cats are the main reservoir. Food animals can become infected via the environment or by ingesting water contaminated with oocysts from infected cat faeces. Reducing exposure to oocysts or tissue cysts in humans can be achieved through (i) cat vaccination (ii) freezing of high-risk meat products and (iii) enhancing biosecurity on pig farms. The different domains and their effects for the different interventions are shown in Table 1 and described below.

2.3.1 | Ad 1

Vaccination of cats may be an effective way to reduce oocyst shedding by cats in the environment (Opsteegh et al., 2015). The intervention will directly influence human infections via oocysts in the environment but also infections via meat as it will reduce the prevalence of infection in livestock. The effects of cat vaccination in animals and humans will be modelled based on available literature or expert opinion.

Unfortunately, no vaccine is commercially available at this moment. However, in a vaccination-challenge experiment, use of a prospective vaccine prevented oocyst shedding in 31 of 37 kittens (Frenkel, Pfefferkorn, Smith, & Fishback, 1991). Depending on the proportion of cats that is domestic and the proportion that is not bound to a certain owner, it may be difficult to reach sufficient vaccination coverage. In this study, we consider both vaccinations of all owned cats or of cats that are kept at livestock farms only. Vaccination of cats can lead to fewer toxoplasma-related abortions in ewes. Most of all, there will be fewer human infections and consequently fewer cost-of-illness and disease burden.

2.3.2 | Ad 2

Freezing meat at -20°C for 2 days will render tissue cysts non-viable (Kotula et al., 1991). Freezing (and thawing) of meat will have effects on the physical quality of meat. The formation of ice crystals during freezing damages the structure in the meat and leads to changes in the biochemical reactions that occur at the cellular level of the meat (Lagerstedt, Enfalt, Johansson, & Lundstrom, 2008; Leygonie, Britz, & Hoffman, 2012). Among other effects, it will lead to changes in moisture loss, colour, and pH, shear force and microbial spoilage (Utrera, Parra, & Estevez, 2014). In general, frozen meat is less juicy and tender, influencing consumers' attitudes towards freezing of meat negatively. Consequently, the price consumers are willing to pay for such products may be affected. Freezing meat will extend the meat production chain and therefore increases the risk of cross-contamination with other pathogens such as *Salmonella* spp. This may happen at the consumer level, but also during the freezing process or via staff at the freezing company. Due to data limitations, the aspect of cross-contamination

TABLE 1 Domains in the society related to the three interventions

Domains	Effects, resulting in changes in costs and benefits	Cat Vaccination	Freezing Meat	Enhancing biosecurity at pig farms
Consumer	<i>Toxoplasma</i> -related patient costs will be assessed	X	X	X
	Consumer surplus ^a		X	
	Consumption of meat may change due to change in meat price		X	
	Costs for cat vaccination	X		
Human health	Health care costs	X	X	X
	Morbidity and premature mortality due to toxoplasmosis are expressed in DALYs. All short- and long-term effects of infection will be included	X	X	X
Producers	Producer surplus ^b . Since we consider freezing meat as an international intervention, the consequences for the producer surplus will be limited as additional costs might spill-through to the consumer.		X	X
	Biosecurity measures will lead to additional costs for pig farmers.			X
	Serological testing in slaughterhouses are additional costs for slaughterhouse that might be put through to the consumer, since we assume that this is an international intervention			X
	Toxoplasmosis is an important cause of abortion among sheep.	X		
	Vaccination of cats at farms can reduce these losses.			
	Facilities at companies will be needed such as freezers, extra surface area and electricity costs. These facilities will have additional annual recurrent costs (e.g. electricity, maintenance) leading to higher productivity costs for slaughterhouses and the meat processing industry.		X	
Employees	<i>Toxoplasma</i> -related productivity losses will be assessed	X	X	X
	Freezing of meat will lead to extra employment.		X	
	The development, campaign, distribution and vaccination of cats will lead to extra employment for veterinarians	X		
	The biosecurity measures will affect employment of pig breeders, and fatteners, but also persons involved in rodent control and persons who perform the audits.			X
Social security, pensions	A change in employment rate will affect social security and pensions.	X	X	X
Education	Less infections will lead to less special education	X	X	X

^aConsumer surplus is an economic measure of consumer benefit, which is calculated by analysing the difference between what consumers are willing and able to pay for a good or service relative to its market price, or what they actually do spend on the good or service. A consumer surplus occurs when the consumer is willing to pay more for a given product than the current market price.

^bProducer surplus is an economic measure of the difference between the amount that a producer of a good receives (the market price) and the minimum amount that he or she would be willing to accept for the good. The difference, or surplus amount, is the benefit that the producer receives for selling the good in the market.

will not be taken into account. Several mechanisms are available to mitigate the effects of freezing and thawing including the use of novel methods of freezing and thawing and modified atmospheric packaging (Leygonie et al., 2012). To reduce costs and increase acceptance of consumers, the freezing meat intervention will only be targeted at high-risk meat products. This will include meat products from animal species with a high prevalence of *T. gondii* such as sheep, and products that are commonly consumed raw or undercooked, such as steak, raw meat-slices and raw meat spreads. To identify the most relevant high-risk meat products, the quantitative microbial risk assessment (QMRA) model developed to attribute predicted *T. gondii* infections to specific meat products will be updated for this SCBA, based on data from the new Dutch National Food Consumption Survey (Opsteegh, Prickaerts, Frankena, & Evers, 2011; Van Rossum et al., 2016). More information on this QMRA model is given in the model section below. Freezing will not affect the farm practice, and we therefore assume no impact of this

intervention on food animal production. We only consider effects on human health.

2.3.3 | Ad 3

Controlled indoor husbandry (housing) has drastically reduced the prevalence of *T. gondii* infection in pigs and is considered an important factor in the decrease in seroprevalence observed in human populations (Opsteegh et al., 2015). As in most European countries, a quality system is established in the Netherlands for the solid production of pork. Independent organizations monitor and assess working procedures and conditions of animal welfare, quality and food safety on pig farms. Everyone in the production chain, from farmer to butcher, can participate in this scheme. An European Food Safety Authority (EFSA) working group has suggested the following controlled housing conditions to prevent *Toxoplasma* infection in pigs (EFSA, 2011b):

1. keeping the animals indoors
2. keeping cats away from stables, feed, and bedding production and storage, more specifically avoid contact of (faeces of) cats with the feed
3. avoiding dead birds and rodents in the feed
4. implementing strict vermin control
5. availability of suitable clean clothing, shoes and protective equipment for employees and visitors; use of separate boots, wheelbarrow and other equipment to avoid bringing soil into the stables
6. providing clean drinking water and blocking access to surface water

These conditions are already partly included in the Dutch quality system (integrated quality control) for pig farms. Serological monitoring can be a tool in detecting farms infected with *T. gondii* (Swanenburg, Boender, Heres, Koeijer, & Wisselink, 2015). Preliminary results of collected sera showed an average of 2% serological prevalence in pigs. Pigs from organic farms had a prevalence of 3.6% (Swanenburg et al., 2015). Also in Italy, anti-*Toxoplasma* antibodies were detected in 2.1% of pig carcasses from intensively reared pigs suggesting for additional on-farm preventive measures (Papini et al., 2017). It seems that at high-risk farms having seropositive pigs, rodent control is less well performed and many of these farms have outside bulk storage of some feed constituents, which may be accessible for rodents and/or cats (Heres et al., 2015). In this SCBA, we assume serological monitoring of pigs at moment of slaughter; seropositive results will lead to an audit and tailor made advice for farmers with for example the imposition of additional rodent control, etc. Stricter biosecurity measures might result in a lower prevalence in pigs, and consequently fewer human infections. A side effect of the better biosecurity measures might be that rodents spoil fewer feed, resulting in lower feed costs.

2.4 | Step 4 define and value benefits

Following step 3 where the effects and impacts of the new policies were defined, monetary values (in Euro) have to be assigned to the benefits of the interventions for the Netherlands. Three models are used to assess these effects with respect to number of infections, transmission of *T. gondii*, and burden of disease (see section 3). Using Havelaar's model, and recent European disability weights, health gains of avoided infections in terms of DALYs averted will be estimated (Haagsma et al., 2015; Havelaar et al., 2012) and valued in monetary terms. Based on the same outcome tree Mangen et al. (2015, 2017) estimated the health care costs, patients' costs and costs in other sectors (i.e. productivity losses and special education). We will use updated estimates for the year 2016 when estimating savings in health care costs, patients' cost as well as gain in productivity and savings regarding special education due to less complications of toxoplasmosis. The monetary value of an averted DALY will be taken from Dutch recommendations for SCBA in the social domain in which the value of a Quality Adjusted Life Year is described. We assume that the monetary value of a DALY corresponds with the monetary value

of the QALY ranging between 50.000 and 100.000 Euro (Koopmans et al., 2016a). The benefits will mostly affect consumers since they experience less *Toxoplasma*-related infections, productivity losses and special education.

2.5 | Step 5 define and value costs

The aim of this step will be to use state-of-the-art valuation methods for carefully costing all resource use involved in the different interventions for the Netherlands. Various approaches will be needed, either using reference values for health care costs (Zorginstituut_Nederland, 2015) or for non-health outcomes (Drost, Paulus, Ruwaard, & Evers, 2013; Koopmans et al., 2016a), or using a relevant valuation method (hedonic pricing or contingent valuation). Intervention costs will be estimated based on literature and via field experts. The price for freezing meat is based on market prices; however, consumers' preferences on frozen meat are unknown. Therefore, we will perform a Discrete Choice Experiment (DCE), a type of contingent valuation in which preferences of consumers can be assessed. The so-called attributes, items that are important for consumers' decisions, will be taken from the literature and interviews with experts. Using a price proxy, we come close to estimation for the willingness to pay for frozen meat (hence, the willingness to pay for avoidance of infection risk) or the amount of compensation consumers may want for frozen meat (hence, the compensation needed to forego consumption of fresh meat). We can use this estimate to determine the consumers' surplus, the monetary value of the benefit that they accrue from consuming types of meat important in the transmission of toxoplasmosis. The costs will initially affect the pig farmers who pay for the enhanced biosecurity, the cat owners who pay for the vaccination (who are in practice also consumers) and the freezing companies for freezing meat. Serological costs will be paid by the slaughterhouse who, we might assume transfer these costs to the consumer. The same applies for the freezing costs which are spilled-over to the consumer, resulting in slightly higher consumer prices.

2.6 | Step 6 assess the net present value

This step considers the summation of the monetized costs and benefits using an Excel model (see section 3) to obtain a net present value in Euros per intervention measure. It also includes presenting a list of different stakeholders involved and provides detailed insight into the gains and losses for the different stakeholders over time.

2.7 | Step 7 conduct sensitivity analyses

Uncertainty is interpreted in a broader sense than merely statistical uncertainty (as represented by 95% intervals). This assessment involves the identification and characterization of all uncertainties of the models using an uncertainty typology (Knol, Petersen, van der Sluijs, & Lebret, 2009). Such a typology helps to characterize uncertainty sources with respect to the place where the source of uncertainties manifested (e.g. study boundaries or in the model structure),

the nature of the uncertainty (lack of knowledge or variability) and its range (probabilistic or scenario-based).

2.8 | Step 8 present outcomes

Here we present a conclusion of the economic consequences for society with respect to the interventions under study. We report the outcomes of both the main analysis and the sensitivity analyses in agreement with the pertinent guideline for reporting economic evaluations in a transparent and replicable way (Husereau et al., 2013). This will be done for each of the interventions under review and include a list of the non-monetized costs and benefits and will be complemented by a research agenda to address the most salient knowledge gaps identified by our study.

Because costs (investments) have to be made now and effects will spread out over many years, it is common in an SCBA to use a time horizon that covers as many costs and effects as possible. A discount rate is used because costs and benefits in the future are valued less than in the present. The time horizon used in our model will be 10 years, and the discount rate of 3% is conform the advice of the Dutch Ministry of Finance (van Ewijk et al., 2015).

3 | THE MODELS

Four different models will be employed to estimate the societal costs and benefits of three different interventions:

3.1 | The QMRA model: relative attribution of meatborne infections in humans

The QMRA makes it possible to quantify the contribution of sheep, pork and beef products to predicted *T. gondii* infections in the Dutch population (Opsteegh et al., 2015). The model takes the following steps: (i) calculating the number of bradyzoites per infected portion, (ii) estimating the reduction by salting, followed by freezing and finally heating, (iii) estimating the probability of human infection per infected portion using a dose-response relation, (iv) multiplying the outcome of c with the prevalence of *T. gondii* per livestock species to estimate the probability of infection per portion and (v). multiplying the probability of infection per portion with the consumed number of portions per year to predict the total number of infections per meat product. The previously published model, which uses consumption data from 1997 and 1998, will be updated with new data from the Dutch National Food Consumption Survey. The incidence of human infections without and with intervention (i.e. freezing, improved biosecurity) will be the outcome of this model, and the estimated difference will be the input for the SCBA model. Improving biosecurity measures on pig farms is assumed to result in a lower prevalence in pigs, and consequently in pork. Since prevalence data on the expected effectiveness of improved biosecurity are still in process in a current project, we will assume that the effectiveness of this intervention will result in a lowered prevalence in pigs and anticipate that the lower

prevalence in pigs results in a lower number of contaminated pork products. This will lead to a lower number of human toxoplasma cases in the QMRA model.

3.2 | The *T. gondii* transmission model in cats and their environment

In an epidemiological model, *T. gondii* transmission with respect to cat vaccination as described by Lelu, Langlais, Poulle, and Gilot-Fromont (2010)) will be modified. This is a so-called SIR-model, a disease compartment model existing of 3 compartments: S=susceptible, I=infectious and R=recovered. The cat population is split into these three compartments, and the prey population (mice) is divided into two compartments, susceptible and infected mice. Because cats are assumed to defecate in the area of their habitat, there is a limited surface that can be contaminated by oocysts. Therefore, the environment exists of two compartments: uncontaminated and contaminated defecating areas. The model will consider different proportions of vaccinated cats, ranging from 0 to 1, to study to what extent these various vaccination levels would reduce the presence of oocysts in the environment. Encountering an infectious oocyst dose is assumed to follow a Poisson process. Therefore, due to the relatively small disease incidence rate, the risk of exposure to any oocyst dose becomes proportional to the number of oocyst present in the environment. By combining a dose-response relation with risk of exposure, we will calculate the expected number of oocyst-driven infections and how their number is reduced with the various vaccination levels. There is no clear human dose-response relation with regard to oocyst exposure, but data from several animal studies suggest that the response is similar among mice, rats and pigs (Dubey, 1996, 2006; Dubey & Frenkel, 1973; Dubey, Speer, Shen, Kwok, & Blixt, 1997; Dubey et al., 1996). We will construct a dose-response relation based on these data as we have no reason to assume that for humans it would be different.

3.3 | Disease burden model

The outcome of infection in terms of diseases caused by *T. gondii* is expressed in DALYs (Havelaar et al., 2012), in which a DALY is the sum of the number of years of life lost (YLL) due to diseases caused by *T. gondii* and the number of years lived with a disability (YLD) caused by *T. gondii* ($DALY = YLL + YLD$). YLL is calculated by summation of all fatal cases due to all health outcomes of *T. gondii* multiplied by the expected individual life span at the age of death. YLD is the sum of outcomes of all cases of which duration of the illness and the disability weights of a disease caused by *T. gondii* are multiplied.

We attribute toxoplasma disease incidence, disease burden and the cost-of-illness to different exposure pathways, based on an expert elicitation study (Havelaar, Galindo, Kurowicka, & Cooke, 2008). This study estimated the fraction of all human cases by five major pathways (i.e. food, environment, direct animal contact, human-human transmission and travel). The foodborne pathway was further subdivided into 11 food groups (e.g. pork, sheep, cattle).

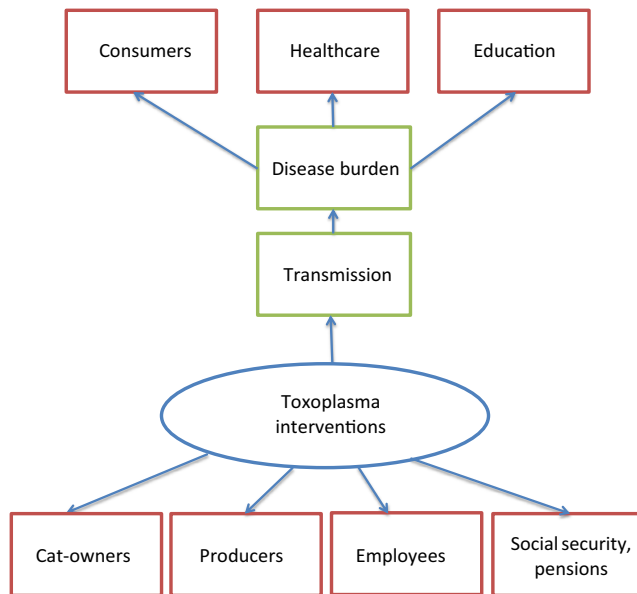


FIGURE 2 Flow chart of the social cost-benefit analysis model. [Colour figure can be viewed at wileyonlinelibrary.com]

3.4 | The SCBA model

The SCBA model is implemented as a Microsoft Excel model. The SCBA model synthesizes all available input from the above-mentioned models. Results are transformed into overall costs and benefits associated with the interventions considered in this project (Figure 2).

The model includes:

1. the costs of implementing (and enforcing) the three different interventions directed at diminishing exposure to *T. gondii*;
2. the effects of the interventions on the exposure to *T. gondii*;
3. the costs and benefits associated with reduced *T. gondii* exposure for the different domains as listed in Table 1.

There are several types of input data to the SCBA model

1. Pig farm data (number of farms, pigs, tested pigs at slaughter, amount of pig feed);
2. Cat population data (owned cats, stray cats and cats at farms);
3. Meat consumption data (annual number of portions of risk meat per person, total amount of consumed risk meat);
4. Cost data (costs with respect to cat vaccination, freezing meat, enhancing biosecurity pig farms as well as healthcare costs, productivity losses and special education costs)
5. Quality of life data (toxoplasma-related disease burden and premature deaths)

The Excel model determines the net costs and benefits of the three interventions by comparing the reference scenario (with no additional policies) with alternative scenarios including reduced *Toxoplasma* transmission by simply calculating the difference between the costs in the alternative and the reference scenario. Net

results are presented per intervention: undiscounted per year, discounted for the 10-year period and also per stakeholder: consumers, freezing meat companies, farmers, slaughterhouses and government.

4 | CONCLUSION

This SCBA will provide evidence on the effectiveness and net benefits of promising interventions targeted at toxoplasmosis. In addition, this study will clarify potential barriers and facilitators of implementation. As toxoplasmosis has a high disease burden and prevention is currently limited to health education for specific risk groups, more effort to reduce transmission of *T. gondii* is warranted. As far as we know this study is the first that investigates the long-term social costs and benefits for society of toxoplasmosis-related preventive interventions. The SCBA will present which intervention leads to the greatest welfare gains and shows who has to pay for these welfare gains and who ultimately benefits most. Both aspects are of importance for policy measures. Since SCBAs in the field of public health are relatively scarce, the study will contribute to our understanding of the feasibility of SCBAs targeted at other zoonoses with high consequences for society. Other challenging issues during this project will be the unravelling of data targeted at avoidance of double counting in the domains affected, as well as the management of impaired data in the several domains of society for valid calculations in the SCBA.

The research described herewith will present a full picture of socio-economic benefits of preventive strategies against a zoonosis with a high disease burden in order to give decision makers recommendations and guidance to reduce morbidity and mortality of toxoplasmosis.

CONFLICT OF INTERESTS

None.

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